Dronabinol

Brand Name: Marinol
Drug Class: Opportunistic Infection and Other Drugs

Drug Description

Dronabinol is synthetic delta-9-tetrahydrocannabinol (delta-9-THC). Delta-9-THC is a naturally occurring component of Cannabis sativa L. (marijuana). [1]

HIV/AIDS-Related Uses

Dronabinol was approved by the FDA on December 23, 1992, for use in the treatment of anorexia-associated weight loss in patients with HIV/AIDS. Tachyphylaxis and tolerance to some effects of dronabinol develop with chronic use; unlike the cardiovascular and central nervous system (CNS) effects, the appetite stimulant effects of dronabinol have been sustained for up to 5 months in AIDS patients receiving doses ranging from 2.5 mg to 20 mg dronabinol daily.[2] [3]

Non-HIV/AIDS-Related Uses

Dronabinol is indicated in selected patients for the prevention of nausea and vomiting associated with emetogenic cancer chemotherapy when other antiemetic medications are not effective.[4]

Pharmacology

The exact mechanism of action of dronabinol is not known. Cannabinoid receptors in neural tissue may mediate the effects of dronabinol and other cannabinoids. Animal studies with other cannabinoids suggest that dronabinol's antiemetic effects may be due to inhibition of the vomiting control mechanism in the medulla oblongata. Central sympathomimetic activity may result in tachycardia or conjunctival injection. Dose-related reversible effects on appetite, mood, cognition, memory, and perception also occur but are subject to great interpatient variability.[5]

Although dronabinol is 90% to 95% absorbed after administration of single oral doses, only 10% to 20% reaches systemic circulation due to first-pass hepatic metabolism and high lipid solubility. Peak concentration is reached 2 to 4 hours after oral administration. Psychoactive effects last 4 to 6 hours; appetite-stimulating effects last at least 24 hours.[6]

Dronabinol binds very highly (97%) to plasma proteins and has a large (approximately 10 L/kg) apparent volume of distribution. Dronabinol is eliminated in a biphasic manner, with an initial half-life of 4 hours and a terminal half-life of 25 to 36 hours. Extensive first-pass hepatic metabolism, primarily by microsomal hydroxylation, yields both active and inactive metabolites. Dronabinol and its principal active metabolite, 11-OH-delta-9-THC, are present in approximately equal concentrations in plasma.[7]

Dronabinol is in FDA Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. Reproduction studies in mice and rats at doses up to 30 times and 20 times the maximum recommended human dose in AIDS patients, respectively, have revealed no evidence of teratogenicity. However, increased fetal mortality, early resorptions, and dose-dependent decreases in weight gain and number of viable pups were observed. Dronabinol is distributed into and concentrated in human breast milk.[8]

Elimination is primarily biliary, with approximately 50% of an oral dose appearing in the feces in 72 hours (less than 5% as unchanged drug); 10% to 15% of the parent drug and metabolites appear in the urine within 72 hours. Following single dose administration, low levels of dronabinol metabolites have been detected for more than 5 weeks in the urine and feces. Prolonged, low-level elimination of dronabinol and its metabolites is attributed to the drug's large and complex volume of distribution.[9] [10]

Adverse Events/Toxicity

Adverse effects observed with use of dronabinol and requiring attention include amnesia, mood changes, delusions, hallucination, depression, anxiety, heart palpitations, and tachycardia. Less serious adverse effects include ataxia, dizziness, drowsiness, euphoria, nausea, trouble thinking, vomiting, asthenia, blurred or otherwise altered vision, dryness of mouth, vasodilation and facial flushing, orthostatic hypotension, and

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Adverse Events/Toxicity (cont.)

restlessness.[11]

Drug and Food Interactions

Concurrent use of dronabinol with alcohol, CNS-depressive medications, or apomorphine may potentiate the depressive effects of dronabinol or these medications. Prior administration of dronabinol may decrease the emetic response to apomorphine. Anticholinergics, antihistamines, and CNS-stimulating medications (especially amphetamines, cocaine, and sympathomimetic agents) may cause additive or synergistic tachycardia and possible cardiotoxicity if used concurrently with dronabinol.[12]

Because dronabinol is highly plasma protein bound, it may displace other protein-bound drugs. Although this displacement has not been confirmed in vivo, practitioners should monitor patients for a change in dosage requirements when administering dronabinol to patients receiving other highly protein-bound drugs.[13]

Contraindications

Dronabinol is contraindicated in any patient with known hypersensitivity to any cannabinoid or to sesame oil. Dronabinol use should be carefully considered in patients with cardiac disorders or hypertension (because of an increased risk of occasional hypotension, new or worsened hypertension, syncope, or tachycardia); a history of substance abuse, including acute alcoholism (because of an increased risk of dronabinol abuse); psychosis, bipolar disorder, mania, depression, or schizophrenia (because dronabinol may exacerbate these conditions); and patients requiring concomitant therapy with sedatives, hypnotics, or other psychoactive drugs (because of potential additive or synergistic CNS effects). Dronabinol should be prescribed to pregnant women, nursing mothers, and pediatric patients with caution; the drug has not been studied in these patient populations. Patients with any of these conditions should be carefully monitored by their physicians because of individual variation in response and tolerance to the effects of dronabinol.[14] [15]

Clinical Trials

For information on clinical trials that involve Dronabinol, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Dronabinol AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[16]

Dosage Form: Dronabinol soft gelatin capsules containing dronabinol 2.5 mg, 5 mg, or 10 mg solution in sesame oil.[17]

Storage: Dronabinol capsules should be packaged in a well-closed container and stored between 8 C and 15 C (46 F and 59 F). Alternatively, dronabinol can be refrigerated, but it should be protected from freezing.[18]

Chemistry

CAS Name:
1-trans-delta9-Tetrahydrocannabinol[19]

CAS Number: 1972-08-3[20]

Molecular formula: C21-H30-O2[21]

C80.21%, H9.62%, O10.18%[22]

Molecular weight: 314.46[23]

Boiling point: 200 C[24]

Physical Description: Dronabinol is a light yellow, resinous oil that is sticky at room temperature and hardens upon refrigeration.[25]

Solubility: Dronabinol is insoluble in water and is formulated in sesame oil.[26]

Other Names

Tetrahydrocannabinol[27]

THC[28]

delta9-THC[29]

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Further Reading

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Manufacturer Information

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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